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05/24/91

☒ This application has been examined ☒ Responsive to communication filed on 16 July 1990 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1 – 70 are pending in the application.
   Of the above, claims 17-29, 34-36, and 41-70 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-16, 30-33, and 37-40 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The application should be reviewed for errors. Examples of the informalities found are as follows: the reference citation of Scores et al. (number 27 at page 47) should be reviewed for accuracy; the "b" and "c" on page 10 referring to the promoter used and enzymatic activity respectively are not found in Table 1.

The application is objected to because of alterations which have not been dated as is required by 37 CFR 1.52(c) and 1.56. A properly executed affidavit or declaration signed by all of the inventors identifying the alterations and stating when the unsigned and/or undated alterations were made is required. If the alterations were made before the signing of the oath or declaration, a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by its Serial Number, filing date and the title is also required. If the alterations were made after the signing of the oath or declarations, a full explanation and cancellation of such alterations is required. Attention is directed to page 8, line 19, page 10, line 24, page 17, lines 30 and 32, page 19, line 23, page 23, line 23, page 24, lines 10 and 24, page 29, lines 13 and 14, page 35, lines 13 and 26, page 39, lines 6 and 8, page 40, line 12, page 41, lines 33 and 34, page 44 (Table 6), which contain initialed but undated corrections to the specification. See also the claims.

The use of what are apparently trademarks has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. The use of trademarks is permissible in patent applications, however, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Attention is directed to at least the following: "diazinon", "paraoxon", "patathion", and "durban". The specification should be reviewed for use of other tradenames/trademarks besides those mentioned.

Correction of the foregoing is required.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16, 30-33 and 37-40, drawn to a bacterial organophosphorous acid anhydrase DNA, an expression vector for the DNA and a transformed microorganism (or in vitro cultured host cell containing the vector for producing organophosphorous acid anhydrase are, for example, classified in at least Class 435, subclasses 91, 172.3, 240.2, 252.33, 252.34, 320.1, and Class 536, subclass 27.

II. Claims 17-19, 34 and 41, drawn to a transgenic organism (i.e. a multicellular organism) are, for example, classified in at least Class 800, subclass 2.

III. Claims 20-29, 35, 36, 42, and 43, drawn to a method for making bacterial organophosphorous acid anhydrase are, for example, classified in at least Class 435, subclasses 69.1, 70.1, and 71.1.

IV. Claims 44-52, drawn to organophosphorous acid anhydrase are, for example, classified in at least Classes 435 and 530, subclasses 183 and 350 respectively.

V. Claims 53-64, drawn to a method of detoxifying an organophosphorous compound by exposure to the organophosphorous acid anhydrase are, for example, classified in at least Class 435, subclasses 41 and 42.

VI. Claims 65 and 66, drawn to a method of detecting bacterial colonies capable of detoxifying organophosphorous acid anhydrides are, for example, classified in at least Class 435, subclass 7.4.

VII. Claims 67-69, drawn to a method of protecting insects by feeding the insects or infecting the insects or its environment with microorganisms which express via a vector an organophosphorous acid anhydrase is, for example, classified in Class 424, subclass 93.

VIII. Claim 70, drawn to a pesticide is, for example, classified in Class 71, subclass 71 and Class 424, subclass 405.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I, and of Groups III, VI and VII are related as product and processes of use. The inventions can be shown to be distinct if

either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). In the instant case, the DNA can be used as a probe, the vectors can be used not only as a probe but also for the production of biologically different compound than the organophosphorous acid anhydrases by substitution of a different gene and the cells can be used as sources of DNA in a process for producing a genomic library all of which are different methods of using the DNA, vectors and host cells from that indicated in the claims of Group III. It is also pointed out that the process of Groups VI and VII are alternative processes of use of the transformed microorganisms of Group I.

Inventions of Groups III and IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different products or (2) that the product as claimed can be made by another and materially different process (MPEP 806.05(f)). In the instant case, the organophosphorous acid anhydrase of Group IV is isolated form the microorganism that naturally produces it (see Lewis et al., BZ and Chiang et al., BE).

Inventions of Group IV and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). In the instant case, the process can be accomplished via the alternative processes of Group VII which recites using an entire microorganism to detoxify the organophosphorous compounds or by basic hyrolysis, dilution in aqueous medium, or incineration (see the specification at page 2). It is pointed out that while the specification indicates the alternative methods are not necessarily efficient, they are, nevertheless alternatives to using the organophosphorous acid anhydrase.

The invention of Group VIII, a pesticide composition is independent and distinct form that of Groups I and IV. Note that the cells, DNA, vectors, and enzyme have different classifications and functions than an organophosphorous based pesticide and organophosphorous acid anhydrase inhibitor. Moreover, a search of the issued patent and published scientific literature would not have been so coextensive as to result in a complete and thorough search of any one other invention as defined by the claim groups. It is also pointed out that the particulars of Groups VI and VII are not required in the practice of the invention of Group V which indicates using only the enzyme per se.

Because these inventions are distinct for the reasons given above and since they have acquired a separate status in the art as shown by their different classification, subject matter, and are separately and independently searched, restriction for examination purposes as indicated is proper.

During a telephone conversation with C. Steven McDaniel on 15 April 1991 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-16, 30-33 and 37-40. Affirmation of this election must be made by applicant in responding to this Office action. Claims 17-29, 34-36 and 41-70 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent; or,

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide a reasonable written description for practicing the claimed

invention. It is pointed out that the specification recites using P. diminuta and a Flavobacterium sp (ATCC 27551) (see the cited references to Harper et al., BX, and McDaniel et al., BY) which set forth DNA sequences coding for opd where the organophosphorous acid anhydrase DNA set forth in Figure 1 of the specification are only partially identical. From the recited examples in the specification, it is not readily apparent that the species of bacteria are any different, that the plasmids used are any different, that the isolated DNA that was sequenced was any different, that the functionality encoded by the DNA is any different, and yet the sequences recited in the Harper et al., McDaniel et al., Mulbry et al. (1) and Figure 1 of the specification set forth different DNA sequences coding for what is apparently the same enzyme. Note that page 21 of the specification recites using the plasmid pCMS1 (fig. 2 of Harper et al.) and sets forth the DNA sequence (fig. 1). This is apparently the same plasmid and DNA as in the specification (compare the paragraph bridging pages 23 and 24 of the specification and the McDaniel et al. reference, see RESULTS). Note also that fig. 4 of the McDaniel reference is identical to fig. 2 of the present application. Thus, there are apparently at least three different references all directed to the apparently identical genetic material where no one reference indicates a sequence identity for the apparently identical genetic material and therefore, a query is raised as to what ~~is~~ genetic material is disclsoed as having the properties of the organophosphorous anhydrase.

Claims 2, 3, 11, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 2 the terminology "extraneous DNA" is vague and indefinite. Is it the non coding sequences shown in the sequence set forth in claim 1 or does it refer to sequences that are not even shown in the claim 1? As set forth in claim 3, it is not clear whether or not the claim refers to the DNA as being a plasmid or that the DNA is originally isolated from for example, a naturally occurring plasmid. Claim 11 is vague and indefinite in reciting "capable" which is only latent capacity. Claim 13 is vague and indefinite with regard to the "microorganism" and "bacteria" (note the singular and the plural).

Claims 7-10, 30-33 are rejected under 35 U.S.C. 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Implicit in the expression vector of claim 6 is the fact that for the vector to be an expression vector, the promoter, start, and termination codons must be present and in proper reading frame else the heterologous DNA would not be properly expressed, thus, claim 7 (note the dependency of claims 8-10) does not further limit claim 6. Claims 30-33 do not further limit claims 1, 6, 12, and 14 because the sequences shown in claims 1, 6, 12, and 14 do not show that there is a sequence which can be deleted. Note that the DNA and the amino acid sequence already starts with the ATG coding for Met.

Claims 1-3, 5-7, 9, 10, 12-13, 30-32, and 37-39 are rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over McDaniel et al. (BY) which discloses cloning and expression of an opd gene encoding a phosphotriesterase using the same strains, vectors, restriction enzymes, and DNA fragment. Note the unexplained disparity of the sequences where given the fact that DNA is apparently the same DNA that was sequenced in the McDaniel et al. reference, the DNA is the same. In the alternative, given the starting materials and teachings in the McDaniel et al. reference, it would have been obvious that the ordinary skilled artisan would have been able using the recited teachings to obtain and alternative gene and sequence. Thus, the reference anticipates the invention as claimed and if not anticipated then obvious.

Claims 1-7, 9, 10, 12-13, 30-32, and 37-39 are rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Harper et al. (BX) which discloses cloning and expression of an opd gene encoding a phosphotriesterase where the DNA sequence is the same for P. diminuta and a Flavobacterium sp (ATCC 27551). Note that the same strains, vectors, restriction enzymes, and DNA fragment are used in the present application and that there is an unexplained disparity of the sequences where given the fact that DNA is apparently the same DNA that was sequenced in the

Harper et al. reference, the DNA is the same. In the alternative, given the starting materials and teachings in the Harper et al. reference, it would have been obvious that the ordinary skilled artisan would have been able using the recited teachings to obtain and alternative gene and sequence. Thus, the reference anticipates the invention as claimed and if not anticipated then obvious.

Claims 1-7, 9, 10, 12-13, 30-32, and 37-39 are rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over either of Wild et al. (AT) or Mulbry et al. (AY). Wild et al. disclose cloning and expression of organophosphate degrading genes from P. diminuta and a Flavobacterium. Mulbry et al. disclose cloning and expression of an organophosphate degrading genes from P. diminuta and a Flavobacterium (ATCC 27551) and point out (page 929) that "it was possible to use a cloned DNA fragment that contained the opd gene isolated from an American strain of P. diminuta to recognize the homologous DNA sequence from a Flavobacterium sp isolated in the Philippines. It is pointed out that while the sequence is not disclosed, in the alternative, only routine sequencing would have been needed to determine the sequence and thus, the invention as claimed is anticipated by the references and if not anticipated then obvious.

Claims 1-7, 9, 10, 12-13, 30-32, and 37-39 are rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over McDaniel (AZ) which discloses cloning and expression of an opd gene encoding a phosphotriesterase using the same strains, vectors, restriction enzymes, and DNA fragment (see at least page iii, the tables, pages 46, 55-56, 69, figs. 17 and 19, 82, 89-91, and 116-120. It is pointed out that while the sequence is not disclosed, in the alternative, such sequencing was performed. Thus, the invention as claimed is anticipated by the reference and if not anticipated then obvious.

Claims 1-3, 5-7, 10, 12-13, 30-32, and 37-39 are rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Serdar et al. (BC) which discloses cloning and expression of a

gene encoding a parathion hydrolase from the vector pCMS1 into pBR322 in E. coli using at least the restriction enzymes pSTI and BamH1 to obtain a DNA fragment. In the alternative, given the starting materials and teachings in the Serdar et al. reference, it would have been obvious that the ordinary skilled artisan would have, using known routine procedures for sequencing a DNA, obtained the DNA sequence. Thus, the reference anticipates the invention as claimed and if not anticipated then obvious.

Claims 1-10, 12-16, 30-33, and 37-40 are rejected under 35 U.S.C. 103 as being unpatentable over Luckow et al. taken with all of Wild et al. (AT), Mulbry et al. (AY), McDaniel (AZ), and Serdar et al. (BC). Luckow et al. disclose that foreign genes are readily expressed using baculoviral vectors and are widely accepted for expression of proteins of agricultural and medical importance (see at least the abstract and the use of S. frugiperda cells, section on EXPERIMENTAL PROTOCOLS) such that one of ordinary skill in the art would have been motivated to use the baculoviral vectors and hosts because the heterologous products produced are biologically active and produce recombinant products very similar to the authentic proteins (page 51) and because the vectors allow "expression of prokaryotic" (here the organophosphorous acid anhydrase DNA, an agriculturally important protein since it catalyzes the transformation of various organophosphorous pesticides) "or eukaryotic genes to produce fused or non-fused recombinant proteins" for the same advantage of "abundant expression of recombinant proteins" (see page 47). While Luckow et al. does not disclose an organophosphorous acid anhydrase DNA such as that described in the Wild et al., Mulbry et al., McDaniel, and Serdar et al., which are applied herein as indicated in the previous grounds of rejection. Luckow et al. as indicated above would have motivated one of ordinary skill in the art to substitute the organophosphorous acid anhydrase DNA into at least the vectors disclosed in the Luckow et al. reference and to use the appropriate host cells. Here the combination of Luckow et al. with all of the Wild et al., Mulbry et al., McDaniel, and Serdar et al. references would have resulted in DNA coding for the organophosphorous acid anhydrase inserted in the appropriate baculoviral and/or bacterial vectors and transformed host cells. Thus, the invention as is now claimed was within the ordinary skill in

the art to make and use at the time it was made; and, was as a whole, clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claim 1-16, 30-33 and 37-40 are rejected under 35 U.S.C. 103 as being unpatentable over Luckow et al. taken with all of Wild et al. (AT), Mulbry et al. (AY), McDaniel (AZ), and Serdar et al. (BC) as applied to claims 1-10, 12-16, 30-33, and 37-40 above, and further in view of Old et al. Old et al. disclose that transposons are broad host range vectors where cloned genes (any DNA) are introduced into Drosophila using transposable P-elements and would have motivated one of ordinary skill in the art to use an alternative system to the baculovirus set forth in the Luckow et al. reference because Old et al. disclose that (page 161) the transposon vector permits the clones genes to be stably inserted into the chromosome. Such a vector could have useful industrial applications for it does not put an extra-genomic genetic load on the recipient cell". Here, the teaching of the agricultural importance of pesticide degradation and that foreign genes are readily expressed using baculoviral vectors and are widely accepted for expression of proteins of agricultural and medical importance as indicated in the combined teachings of the Luckow et al., Wild et al., Mulbry et al., McDaniel, and Serdar et al. disclosures would have motivated one of ordinary skill in the art to modify the combined teachings of Luckow et al., Wild et al., Mulbry et al., McDaniel, and Serdar et al. by also using a transposon that modifies the Drosophila genome to broaden the host range of the modified vectors. Thus, the invention as is now claimed was within the ordinary skill in the art to make and use at the time it was made; and, was as a whole, clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Inquiry regarding this communication should be directed to Christopher Low at telephone number (703) 308-0196.

CSF
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16 April 1991

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